Remarks/Arguments

Favorable consideration of this application is respectfully requested in view of the following remarks.

Claims 21 and 25-33 are pending in the application. Claims 21, 26, 27 and 29-31 have been rejected under 35 USC 103(a) as being unpatentable over WO 94/28902 in view of Sui et al (US 6, 077,841). Claims 25, 28, 32 and 33 are rejected under 35 USC 103(a) as being unpatentable over WO 94/28902 in view of Sui (US 6, 077,841) and further in view of Purewal et al (US 5,225,183).

The Rejection of Claims 21, 26, 27 and 29-31 Under 35 U.S.C. §103(a), May Properly Be Withdrawn

Claims 21, 26, 27 and 29-31 have been rejected under 35 U.S.C. §103(a) as being unpatentable over WO 94/28902 in view of Sui et al. (U.S. 6,077,841). Before addressing the rejection based on these references, a brief summary of the invention as defined in independent Claim 21 is stated below.

Independent Claim 21 is directed to a method of treating sexual dysfunction which comprises administering by inhalation an effective amount of an inhibitor in an atomisable composition or a finely divided particulate form. The inhibitors are selected from the group consisting of 5-[2-ethoxy-5-(4-methylpiperazinyl-sulfonyl)phenyl]-1-methyl-3-*n*-propyl-1,6-dihydro-*7H*-pyrazolo[4,3-*d*]-pyrimidin-7-one, 4-phenylmethylamino-6-chloro-2-(1-imidazolyl)quinazoline, 4-phenyl-methylamino-6-chloro-2-(3-pyridyl)-quinazoline, 1,3-dimethyl-6-(2-propoxy-5-methane-sulfonylamidophenyl)-1,5-dihydropyrazolo[3,4-*d*]pyrimidin-4-one and 1-cyclopentyl-3-ethyl-6-(3-ethoxy-4pyridyl)-pyrazolo[3,4-*d*]pyrimidin-4-one.

These specific inhibitors are particularly beneficial to the user since they exhibit maximum concentration in plasma in a very short time when they are delivered to the lungs. For example, in Example 93 the concentration of sildenafil was shown to reach a maximum within 5 minutes after intratracheal administration to a rat and in Example 94 sildenafil was shown to reach a maximum concentration in plasma within 2 minutes after intratracheal administration to a rat.

WO 94/28902 is directed to the use of a series of pyrazolo[4,3-d]pyrimidin-7-ones, inhibitors of cGMP phosphodiesterases for the treatment of impotence. Included in a list of preferred compounds is Sildenafil, i.e. 5-[2-ethoxy-5-(4-methyl-1-piperazinylsulfonyl)-phenyl]-1-methyl-3-n-propyl-1,6-dihydro-7H-pyrazolo[4,3-d]-pyrimidin-7-one. Oral administration is the preferred route of

administration, but parenteral administration is also suggested (page 10, paragraph 4). There is **no** suggestion or guidance that these compounds may be administered via inhalation.

Sui et al. is directed to the use of 5-**heterocyclyl** pyrazolopyrimidinones and derivatives thereof for the treatment of male erectile dysfunction (ED). In particular, Sui et al. in the background section describe the shortcomings of utilizing the phosphodiesterase V (PDEV) inhibitor, Sildenafil and related analogs, as an orally effective medication to treat ED, i.e., that Sildenafil and analogs thereof have less efficacy in patients who had undergone a radical prostatectomy and that they possess undesirable side effects including headache, flushing and disrupted color vision (see column 2, lines 3-13). To address these shortcomings, **Sui et al. describe an alternative class of PDEV inhibitors, 5-heterocyclyl pyrazolo-pyrimidines to treat ED.** While Sui et al. indicate that **5-heterocyclyl pyrazolo-pyrimidines** can be administered through various routes including inhalation, the reference does not teach or suggest that sildenafil, or its analogs can also be administered in inhalable form, the form such an inhalable product would take and how such form of sildenafil would be prepared. Indeed, Sui et al., in its disclosure of the shortcomings of sildenafil in orally administrable form and its provision of 5-HPs in place of sildenafil or its related analogs, discourage the use of sildenafil and its analogs in its orally administrable form let alone in inhalable form. Additionally, Sui et al. does not teach or suggest any of the other compounds recited in amended Claim 21, that such compounds can also be administered by inhalation, the form that such compounds would take or how they would be prepared. In essence, **the teaching of Sui et al. is that in order to overcome the shortcomings/side effects of Sildenafil and its analogs, one of skill in the art should look to new and different compounds, not to new modes of administration for Sildenafil and its analogs**

The Examiner, in rejecting these claims, has asserted that one of ordinary skill in the art would have been motivated to select the compounds of WO94/28902 and then to look "in the art for preferred routes of administration for such agents as taught by Sui et al." Applicants disagree with this assertion. It is reiterated that the thrust of the teaching of Sui et al. is **away** from the compounds of WO94/28902 and **toward** new and different compounds in order to overcome the undesirable side effects of sildenafil and its analogs. There is no teaching or any motivation in Sui et al. to look for a new mode of administration for sildenafil and its analogs. Nor is there any teaching or motivation in Sui et al. to administer, via inhalation, an effective amount of sildenafil and its analogs in order to treat sexual dysfunction.

Additionally, Applicants note that the medication is taken to enable the user to achieve or maintain an erection for sexual intercourse so one skilled in the art would expect the market instead to demand a more discrete method of administration. To this end, Sui et al. acknowledges (column

1, lines 51-59) that mechanical devices are not favored and tend to be used only as a last resort. Sui et al. also acknowledges (column 1, lines 60 through column 2, lines 16) that sildenafil as an orally administrable medication has been welcomed by patients despite causing side effects as discussed above. In not disclosing the form of the inhalable 5-HP product or its preparation, and by exemplifying oral administration of 5-HP Sui et al. recognizes that the market is demanding oral administration. If the market is demanding an effective orally administrable treatment where is the motivation to develop an inhalable seldenfil or other compounds recited in amended Claim 21?

In view of the lack of teaching or suggestion in Sui et al. that sildenafil or the other compounds recited in amended Claim 21 can be effectively administered by inhalation, and the market demand for an orally administrable treatment for ED rather than use of a mechanical device, one skilled in the art would not have been motivated to develop sildenafil and the other compounds of amended Claim 21 in inhalable form to treat ED.

Accordingly, WO94/28902 in view of Sui et al. does not make obvious Claims 21, 26, 27 and 29-31. In view of the above, withdrawal of the rejection of Claims 21, 26, 27 and 29-31 under 35 U.S.C. §103 is respectfully requested.

II. The Rejection of Claims 25, 28 and 32-33 under 35 U.S.C. §103(a) May Properly Be Withdrawn

Claims 25, 28 and 32-33 have been rejected under 35 U.S.C. §103(a) as being unpatentable over WO 94/28902 in view of Sui et al.(US 6,077,841) and further in view of Purewal et al. (U.S. Patent No. 5,225,183).

With respect to WO94/28902 in view of Sui et al., Applicant reiterates the arguments proffered with respect to addressing the rejection of Claims 21, 26, 27 and 29-31.

Purewal et al. is directed to an aerosol formulation which utilizes a particular propellant, 1,1,1,2-tetrafluoromethane, as an ozone-friendly alternative to deliver bronchodilator drugs and steroids to the airways of asthmatic patients. While Purewal et al. describe different types of medicaments that can be utilized with this formulation, it does not teach or suggest that any of the specific compounds recited in amended Claim 21 can be utilized in such a formulation to treat ED.

Accordingly, since one skilled in the art reading WO 94/28902 in view of Sui et al. would not have been motivated to utilize an inhalable form of the specific compounds recited in Claim 21, and Purewal merely teaches the use of an ozone-friendly propellant in an aerosol formulation, the combination of WO 94/28902 in view of Sui et al. and further in view of Purewal does not make obvious Claims 25, 28 and 32-33.

In view of the above, withdrawal of the rejection of Claims 25, 28 and 32-33 under 35 U.S.C. §103(a) is respectfully requested.

In view of the foregoing, it is respectfully submitted that the claims of the instant invention are patentable over WO 94/28902 in view of Sui et al (US 6,077,841) and further in view of Purewal (US 5,225,183) and allowance of the claims is earnestly solicited

Respectfully submitted,

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